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FILE 'BIOSIS' ENTERED AT 10:34:02 ON 15 APR 2003
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=> s integrin antagonist
L9          633 INTEGRIN ANTAGONIST

=> s breast cancer
L10      178471 BREAST CANCER

=> s l9 and l10
L11           0 L9 AND L10

=> s vitronectin
L12        9455 VITRONECTIN

=> s l10 and l12
L13         127 L10 AND L12

=> s l10 (S) l12
L14          61 L10 (S) L12

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15           40 DUP REM L14 (21 DUPLICATES REMOVED)
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=> d ibib abs 35-40

L15 ANSWER 35 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:263650 BIOSIS
DOCUMENT NUMBER: PREV199598277950
TITLE: Site-directed mutagenesis of the arginine-glycine-aspartic acid sequence in osteopontin destroys cell adhesion and migration functions.
AUTHOR(S): Xuan, Jian-Wu; Hota, Charulata; Shigeyama, Yoichiro; D'Errico, John A.; Somerman, Martha J.; Chambers, Ann F.
CORPORATE SOURCE: London Regional Cancer Cent., 790 Commissioners Road East, London, ON N6A 4L6 Canada
SOURCE: Journal of Cellular Biochemistry, (1995) Vol. 57, No. 4, pp. 680-690.
ISSN: 0730-2312.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Osteopontin (OPN) is a secreted calcium-binding phosphoprotein produced in a variety of normal and pathological contexts, including tissue mineralization and cancer. OPN contains a conserved RGD (arg-gly-asp) amino acid sequence that has been implicated in binding of OPN to cell surface integrins. To determine whether the RGD sequence in OPN is required for adhesive and chemotactic functions, we have introduced two site-directed mutations in the RGD site of the mouse OPN cDNA, in which the RGD sequence was either deleted or mutated to RGE (arg-gly-glu). In order to test the effect of these mutations on OPN function, we expressed control and mutated mouse OPN in E. coli as recombinant glutathione-S-transferase (GST)-OPN fusion proteins. Control mouse GST-OPN was functional in cell adhesion assays, supporting attachment and spreading of mouse (malignant PAP2 ras-transformed NIH 3T3, and, to a lesser extent, normal NIH 3T3 fibroblasts) and human (MDA-MB-435 **breast cancer**, and normal gingival fibroblast) cells. In contrast, neither of the RGD-mutated OPN proteins ("delRGD" or "RGE") supported adhesion of any of the cell lines, even when used at high concentrations or for long assay times. GRGDS (gly-arg-gly-asp-ser) peptides inhibited cell adhesion to intact GST-OPN, as well as to fibronectin and **vitronectin**. In chemotaxis assays, GST-OPN promoted directed cell migration of both malignant (PAP2, MDA-MB-435) and normal (gingival fibroblast, and NIH 3T3) cells, while RGD-mutated OPN proteins did not. Together these results suggest that the conserved RGD sequence in OPN is required for the majority of the protein's cell attachment and migration-stimulating functions.

L15 ANSWER 36 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:223622 BIOSIS
DOCUMENT NUMBER: PREV199598237922
TITLE: Growth and metastasis of human breast cancers in athymic nude mice.
AUTHOR(S): Murthy, M. Satya (1); Scanlon, Edward F.; Jelachich, Mary Lou; Klipstein, Sigal; Goldschmidt, Robert A.
CORPORATE SOURCE: (1) Cell Biol. Lab., Dep. Surg. Med., Evanston Hosp. Corp., 2650 Ridge Ave., Evanston, IL 60201 USA
SOURCE: Clinical & Experimental Metastasis, (1995) Vol. 13, No. 1, pp. 3-15.
ISSN: 0262-0898.
DOCUMENT TYPE: Article
LANGUAGE: English
AB To evaluate critically the merit of utilizing a wound model for growing human tumors, a series of increasingly difficult human tumor types were tested for growth at sites of trauma in athymic nude mice. In vitro tumor lines as well as fresh tumors from the breast, colon, rectum, lung, and a

metastasis from an unknown primary were intraperitoneally injected into mice subjected to intra-abdominal organ injury. Successful xenografts were obtained from nine of 10 cell lines and 14 of 24 fresh tumors. The latter included five of six (83%) colon cancers, one lung tumor, metastatic tumor of unknown primary, three of four (75%) metastatic **breast cancers** and four of six (67%) estrogen receptor (ER)-negative breast primary tumors. Six ER-positive breast tumors tested failed to grow in mice without estrogen supplementation. Xenografts from two breast, two colon and the lung cancers formed spontaneous metastases and all xenografts tested were able to yield serial transplants in the surgical wound model. Histologically, all xenografts and their metastases were identical to their respective donor tumors. Transplantability in mice without exogenous estrogen supplementation was linked to the absence of estrogen and progesterone receptors in breast tumors. Transplantability of the cell lines was associated with the expression of cell surface receptors for fibronectin and hyaluronic acid. Receptors for other extracellular matrix components, namely, laminin, **vitronectin**, collagen, fibrinogen or von Willebrand factor were not associated with transplantability. These results demonstrate that a large proportion of human tumors, including the breast tumors, can be successfully xenografted into athymic mice by providing them with a healing wound environment, and that such xenografts grown at ectopic sites exhibit metastatic ability.

L15 ANSWER 37 OF 40 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 93013762 MEDLINE
DOCUMENT NUMBER: 93013762 PubMed ID: 1383121
TITLE: Integrins and their accessory adhesion molecules in mammary carcinomas: loss of polarization in poorly differentiated tumors.
AUTHOR: Pignatelli M; Cardillo M R; Hanby A; Stamp G W
CORPORATE SOURCE: Department of Histopathology, Royal Postgraduate Medical School, Hammersmith Hospital, London, UK.
SOURCE: HUMAN PATHOLOGY, (1992 Oct) 23 (10) 1159-66.
Journal code: 9421547. ISSN: 0046-8177.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199210
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 20000303
Entered Medline: 19921028

AB The integrins are alpha beta heterodimeric transmembrane proteins mediating cell-substratum as well as cell-cell interactions. To identify the pattern of expression of the beta 1, beta 3, and beta 4 integrins and their accessory adhesion molecules in relation to the malignant phenotype of invasive **breast cancer**, we performed an immunohistochemical study for the alpha 2 beta 1 (VLA-2), alpha 6 beta 1 (VLA-6), alpha v and alpha v beta 3 (**vitronectin** receptor), alpha 6 beta 4, carcinoembryonic antigen, and carcinoembryonic antigen-related molecules in a series of 37 invasive breast carcinomas. All integrin chains examined showed similar patterns in nonneoplastic breast tissue, with strong membrane staining of the myoepithelial cells and weak to moderate staining on the basolateral surfaces of the luminal cells. We found that downregulation of the alpha 2 chain of VLA-2 occurs more frequently in poorly differentiated grade III invasive ductal carcinomas (IDCs) (P = .048). Loss of alpha 6 beta 4 seems also to occur more frequently in grade III IDC (seven of 11 cases, 63.6%) than in grade I/II IDC (two of eight cases, 25%), although this did not reach statistical significance. Carcinoembryonic antigen and carcinoembryonic antigen-related antigens, which are known to function as accessory adhesion molecules, were found mainly in the cytoplasm of neoplastic cells

and there was reduced membrane polarization in poorly organized tumors. In contrast the alpha v beta 3, vitronectin receptor heterodimer recognized by the 23C6 monoclonal antibody was weak or absent in normal breast epithelium, and was weakly expressed in two of 19 (10%) IDCs and in nine of 18 (50%) invasive lobular carcinomas (P = .008). However, the alpha v chain detected with the antibody 13C2 was weakly to moderately expressed on nonneoplastic epithelium and at a similar intensity in 13 of 19 IDCs and 15 of 17 invasive lobular carcinomas, suggesting that in IDC the alpha v chain may be associated with a different beta chain (possibly beta 1 or beta 5). No correlation between integrin expression and estrogen/progesterone receptor status was found. These data provide further evidence that in invasive breast carcinomas there is a widespread deregulated expression of integrins and their accessory adhesion molecules with loss of polarization. Changes in the expression and function of cell adhesion molecules, which control growth and differentiation, may have clinical relevance in the behavior of breast cancer.

L15 ANSWER 38 OF 40 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 92254922 MEDLINE
DOCUMENT NUMBER: 92254922 PubMed ID: 1374587
TITLE: Persistent complement activation on tumor cells in breast cancer.
AUTHOR: Niculescu F; Rus H G; Retegan M; Vlaicu R
CORPORATE SOURCE: Medical Clinic No. 1, Cluj-Napoca, Romania.
CONTRACT NUMBER: F05 TW04624 (FIC)
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1992 May) 140 (5) 1039-43. Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19970203
Entered Medline: 19920611

AB The neoantigens of the C5b-9 complement complex, IgG, C3, C4, S-protein/**vitronectin**, fibronectin, and macrophages were localized on 17 samples of **breast cancer** and on 6 samples of benign breast tumors using polyclonal or monoclonal antibodies and the streptavidin-biotin-peroxidase technique. All the tissue samples with carcinoma in each the TNM stages presented C5b-9 deposits on the membranes of tumor cells, thin granules on cell remnants, and diffuse deposits in the necrotic areas. When chemotherapy and radiation therapy preceded surgery, C5b-9 deposits were more intense and extended. The C5b-9 deposits were absent in all the samples with benign lesions. S-protein/vitronectin was present as fibrillar deposits in the connective tissue matrix and as diffuse deposits around the tumor cells, less intense and extended than fibronectin. IgG, C3, and C4 deposits were present only in carcinoma samples. The presence of C5b-9 deposits is indicative of complement activation and its subsequent pathogenetic effects in breast cancer.

L15 ANSWER 39 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:475167 BIOSIS
DOCUMENT NUMBER: BA94:106542
TITLE: TRANSFORMING GROWTH FACTOR-BETA ENHANCES CALCITONIN-INDUCED CYCLIC AMP PRODUCTION AND THE NUMBER OF CALCITONIN RECEPTORS IN LONG-TERM CULTURES OF HUMAN UMBILICAL CORD BLOOD MONOCYTES IN THE PRESENCE OF 1 25 DIHYDROXYCHOLECALCIFEROL.
AUTHOR(S): MBALAVIELE G; ORCEL P; BOUIZAR Z; JULLIENNE A; DE VERNEJOUL M C

CORPORATE SOURCE: INSERM U349, CENTRE VIGGO PETERSEN, HOPITAL LARIBOISIERE, 75010 PARIS, FRANCE.
SOURCE: J CELL PHYSIOL, (1992) 152 (3), 486-493.
CODEN: JCLLAX. ISSN: 0021-9541.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Transforming growth factor-.beta. (TGF-.beta.) is a multifunctional polypeptide, abundant in bone, that regulates both proliferation and differentiation of a wide variety of cells, but its role in osteoclast differentiation remains controversial. We have recently shown that long-term cultures of human cord blood monocytes, in the presence of 1,25 dihydroxycholecalciferol (1,25-(OH)2D3), give rise to cells that express two markers of the osteoclast phenotype, namely, the **vitronectin** receptor (VNR) and the calcitonin receptor (CTR). TGF-.beta. enhanced the proportion of cells expressing the VNR. In the present study, we investigated the effect of TGF-.beta. on the expression of CTR in cord blood monocytes cultured during 3 weeks in the presence of 1,25-(OH)2D3. When added within the first 2 weeks of culture, TGF-.beta. (500 pg/ml) significantly decreased the cell protein content. TGF-.beta. alone did not stimulate basal cAMP production. The 10 nM-sCT-stimulated cAMP production was enhanced by increasing TGF-.beta. concentrations from 50 pg/ml to 1,000 pg/ml: for 500 pg/ml TGF-.beta., it was 294 .+-. 28% vs. 140 .+-. 25% for control cultures ($p < 0.01$). The sCT dose-response curves showed a higher cAMP production from 10-9 M to 10-7 M of sCT in the presence of 500 pg/ml TGF-.beta. than in control cultures. The increase was 325 .+-. 36% in the presence of TGF-.beta. and 195 .+-. 13% in the absence of TGF-.beta., for 10-7 M sCT ($p < 0.01$). This effect of TGF-.beta. on cAMP production was not observed either when it was added to monocyte cultures the last day or 2 hours before the end of the culture or in MCF7, a human **breast cancer** cell line that expresses CTR. [125I]-sCT binding studies performed on confluent cells showed similar Kd in control and TGF-.beta.-treated cells. By contrast, the CTR number was significantly increased in the presence of TGF-.beta.: 6.1 .+-. 2 .times. 104 receptors per cell in control cultures and 28.8 .+-. 8.1 .times. 104 receptors per cell in TGF-.beta.-treated cultures ($p < 0.05$). It is thus suggested that TGF-.beta. increase the number of CTR of these cells that have other features of preosteoclasts. The role of this cytokine on the process of osteoclast differentiation and in bone resorption is thus emphasized.

L15 ANSWER 40 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1991:29103 BIOSIS
DOCUMENT NUMBER: BA91:18454
TITLE: CHEMOTHERAPY ENHANCES ENDOTHELIAL CELL REACTIVITY TO PLATELETS.
AUTHOR(S): BERTOMEU M C; GALLO S; LAURI D; LEVINE M N; ORR F W; BUCHANAN M R
CORPORATE SOURCE: MCMASTER UNIV., DEP. PATHOL., 1200 MAIN ST. WEST, HAMILTON, ONTARIO, CANADA L8N 3Z5.
SOURCE: CLIN EXP METASTASIS, (1990) 8 (6), 511-518.
CODEN: CEXMD2. ISSN: 0262-0898.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Recent studies indicate that chemotherapy is a cause for thrombosis in **breast cancer** patients. We performed experiments to determine whether the enhanced thrombosis was due, in part, to an effect of chemotherapy on endothelial cell reactivity. Heparinized blood samples were obtained from stage II **breast cancer** patients receiving monthly adjuvant chemotherapy consisting of cyclophosphamide, epirubicin and 5-fluorouracil. Cultured human endothelial cells were incubated with the plasmas for 2 h, and then the reactivity of the endothelial cells to normal donor platelets was determined isotopically.

Endothelial cell reactivity was increased when the endothelial cells were incubated with the postchemotherapy plasmas. The plasma effect persisted after the chemotherapy drugs were cleared from the circulation, but this plasma effect was abolished when the plasmas were heat-inactivated. Furthermore, the increase in endothelial cell reactivity correlated with the level of interleukin-1 present in the postchemotherapy plasma. Finally, the increased endothelial cell reactivity was inhibited by the GRGDS peptide, or by an antibody to the endothelial cell **vitronectin** receptor. These observations suggest that chemotherapeutic drugs alter endothelial cell reactivity to platelets by inducing the release of interleukin-1 which, in turn, facilitates adhesion molecule expression on the endothelial cell surface. If so, these observations provide a possible explanation for one mechanism which may contribute to the thrombogenic effect seen in **breast cancer** patients undergoing chemotherapy.

=> d ibib abs 20-25

L15 ANSWER 20 OF 40 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001042343 MEDLINE
DOCUMENT NUMBER: 20419185 PubMed ID: 10966001
TITLE: Contortrostatin, a dimeric disintegrin from Agkistrodon contortrix contortrix, inhibits breast cancer progression.
AUTHOR: Zhou Q; Sherwin R P; Parrish C; Richters V; Groshen S G; Tsao-Wei D; Markland F S
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Southern California, Keck School of Medicine/Norris Comprehensive Cancer Center, Los Angeles 90033, USA.
CONTRACT NUMBER: P30 CA14089 (NCI)
SOURCE: BREAST CANCER RESEARCH AND TREATMENT, (2000 Jun) 61 (3) 249-60.
Journal code: 8111104. ISSN: 0167-6806.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001207

AB We report the results of a multidisciplinary study on the inhibitory effect of a snake venom disintegrin, contortrostatin, a 13.5 kDa homodimeric protein isolated from Agkistrodon contortrix contortrix (southern copperhead) venom, on breast cancer progression. We demonstrate that contortrostatin binds to integrins and blocks the adhesion of human **breast cancer** cells (MDA-MB-435) to extracellular matrix (ECM) proteins including fibronectin and **vitronectin**, but it has no effect on adhesion of the cells to laminin and Matrigel. Contortrostatin also prevents invasion of MDA-MB-435 cells through an artificial Matrigel basement membrane. Daily local injection of contortrostatin (5 microg per mouse per day) into MDA-MB-435 tumor masses in an orthotopic xenograft nude mouse model inhibits growth of the tumor by 74% ($p = 0.0164$). More importantly, it reduces the number of pulmonary macro-metastasis of the breast cancer by 68% ($p < 0.001$), and micro-metastasis by 62.4% ($p < 0.001$). Contortrostatin is not cytotoxic to cancer cells, and does not inhibit proliferation of the breast cancer cells in vitro. However, contortrostatin inhibits angiogenesis induced by the breast cancer, as shown by immunohistochemical quantitation of the vascular endothelial cells in tumor tissue removed from the nude mice. We have identified alpha(v)beta3, an important integrin mediating cell

motility and tumor invasion, as one of the binding sites of contortrostatin on MDA-MB-435 cells. We conclude that contortrostatin blocks alpha(v)beta3, and perhaps other integrins, and thus inhibits in vivo progression.

L15 ANSWER 21 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:162205 BIOSIS
DOCUMENT NUMBER: PREV200000162205
TITLE: Neovascular targeting with cyclic RGD peptide (cRGDf-ACHA) to enhance delivery of radioimmunotherapy.
AUTHOR(S): DeNardo, Sally J. (1); Burke, Patricia A.; Leigh, Bryan R.; O'Donnell, Robert T.; Miers, Laird A.; Kroger, Linda A.; Goodman, Simon L.; Matzku, Siegfried; Jonczyk, Alfred; Lamborn, Kathleen R.; DeNardo, Gerald L.
CORPORATE SOURCE: (1) Section of Radiodiagnosis and Therapy, Department of Internal Medicine, University of California Davis Medical Center, Sacramento, CA USA
SOURCE: Cancer Biotherapy & Radiopharmaceuticals., (2000) Vol. 15, No. 1, pp. 71-79.
ISSN: 1084-9785.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Radioimmunotherapy (RIT) has been hampered by delivery of only a small fraction of the administered dose of radiolabeled MAb to tumor. A strategy for creating and controlling tumor vascular permeability would enable more effective RIT. The alphavbeta3 integrin receptor is an appealing target for strategies designed to enhance permeability of tumor vessels because it is highly and preferentially expressed in most tumors. In human tumor mouse models, apoptosis of neovascular endothelial cells has been demonstrated after treatment with alphavbeta3 antagonists. Since this apoptotic effect could transiently increase permeability of tumor blood vessels, radiolabeled antibodies (MAb) circulating during this period would have increased access to extravascular tumor. To determine if this hypothesis was correct, a pharmacokinetic study of an immunospecific MAb given after an alphavbeta3 antagonist was performed in nude mice bearing human **breast cancer** xenografts. The alphavbeta3 antagonist, cyclic RGD pentapeptide (c-RGDf-ACHA; cyclo arginine glycine aspartic acid D-phenylalanine -1 amino cyclohexane carboxylic acid), inhibits alphavbeta3 binding to its **vitronectin** ligand at nanomolar levels. Cyclic RGD peptide (250 mug i.p.) given 1 hour before 111In-ChL6 MAb resulted in a 40 - 50% increase in tumor uptake (concentration), when compared to the control tumor uptake, of MAb 24 hours after administration. When cyclic RGD peptide was given as a continuous infusion (17.5 mug/hr) for 1 or 24 hours before 111In-ChL6, tumor uptake of 111In-ChL6 was increased less, and, these data were not statistically different from the control data. There were no differences for any of the groups in the concentrations of 111In-ChL6 in normal organs or blood when compared to the control group. The results suggest that cyclic RGD peptide provided a temporary, selective increase in tumor vascular permeability, that allowed a larger fraction of the 111In-ChL6 to accumulate in the tumor.

L15 ANSWER 22 OF 40 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 2000005706 MEDLINE
DOCUMENT NUMBER: 20005706 PubMed ID: 10537314
TITLE: Urokinase receptor interacts with alpha(v)beta5 **vitronectin** receptor, promoting urokinase-dependent cell migration in **breast cancer**.
AUTHOR: Carriero M V; Del Vecchio S; Capozzoli M; Franco P; Fontana L; Zannetti A; Botti G; D'Aiuto G; Salvatore M; Stoppelli M P

CORPORATE SOURCE: National Cancer Institute, Naples, Italy..
stoppelli@iigbna.iigb.na.cnr.it
SOURCE: CANCER RESEARCH, (1999 Oct 15) 59 (20) 5307-14.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991110

AB Perturbation of adhesive interactions at cell-substratum and cell-cell contact sites is a critical event in the multistep process of cancer invasion. Recent studies indicate that the urokinase receptor (uPAR) is associated in large molecular complexes with other molecules, such as integrins. To test the possibility that uPAR may physically and functionally interact with vitronectin (Vn) receptors, we determined the expression level of uPAR, alpha(v)beta3, and alpha(v)beta5 Vn receptors in 10 human breast carcinomas. Here, we show the ability of uPAR to physically associate with alpha(v)beta5 in the breast carcinomas examined. The functional effects of this interaction were studied using HT1080 human fibrosarcoma and MCF-7 human breast carcinoma cell lines, both exhibiting a urokinase-dependent physical association between uPAR and alpha(v)beta5. Both cell lines respond to urokinase or to its noncatalytic amino-terminal fragment by exhibiting remarkable cytoskeletal rearrangements that are mediated by alpha(v)beta5 and require protein kinase C activity. On the contrary, binding of Vn to alpha(v)beta5 results in the protein kinase C-independent formation of F-actin containing microspike-type structures. Furthermore, alpha(v)beta5 is required for urokinase-directed, receptor-dependent MCF-7 and HT1080 cell migration. These data show that uPAR association with alpha(v)beta5 leads to a functional interaction of these receptors and suggest that uPAR directs cytoskeletal rearrangements and cell migration by altering alpha(v)beta5 signaling specificity.

L15 ANSWER 23 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:484086 BIOSIS
DOCUMENT NUMBER: PREV199900484086
TITLE: Myosin light chain kinase functions downstream of Ras/ERK to promote migration of urokinase-type plasminogen activator-stimulated cells in an integrin-selective manner.
AUTHOR(S): Nguyen, Diem H. D.; Catling, Andrew D.; Webb, Donna J.; Sankovic, Mauricio; Walker, Lori A.; Somlyo, Avril V.; Weber, Michael J.; Gonias, Steven L. (1)
CORPORATE SOURCE: (1) Department of Pathology, Department of Biochemistry and Molecular Genetics, University of Virginia Health Sciences Center, Charlottesville, VA, 22908 USA
SOURCE: Journal of Cell Biology, (July 12, 1999) Vol. 146, No. 1, pp. 149-164.
ISSN: 0021-9525.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Urokinase-type plasminogen activator (uPA) activates the mitogen activated protein (MAP) kinases, extracellular signal-regulated kinase (ERK) 1 and 2, in diverse cell types. In this study, we demonstrate that uPA stimulates migration of MCF-7 **breast cancer** cells, HT 1080 fibrosarcoma cells, and uPAR-overexpressing MCF-7 cells by a mechanism that depends on uPA receptor (uPAR)-ligation and ERK activation. Ras and MAP kinase kinase (MEK) were necessary and sufficient for uPA-induced ERK activation and stimulation of cellular migration, as demonstrated in experiments with dominant-negative and constitutively

active mutants of these signaling proteins. Myosin light chain kinase (MLCK) was also required for uPA-stimulated cellular migration, as determined in experiments with three separate MLCK inhibitors. When MCF-7 cells were treated with uPA, MLCK was phosphorylated by a MEK-dependent pathway and apparently activated, since serine-phosphorylation of myosin II regulatory light chain (RLC)was also increased. Despite the transient nature of ERK phosphorylation, MLCK remained phosphorylated for at least 6 h. The uPA-induced increase in MCF-7 cell migration was observed selectively on **vitronectin**-coated surfaces and was mediated by a beta1-integrin (probably alphavbeta1) and alphavbeta5. When MCF-7 cells were transfected to express alphavbeta3 and treated with uPA, ERK was still phosphorylated; however, the cells did not demonstrate increased migration. Neutralizing the function of alphavbeta3, with blocking antibody, restored the ability of uPA to promote cellular migration. Thus, we have demonstrated that uPA promotes cellular migration, in an integrin-selective manner, by initiating a uPAR-dependent signaling cascade in which Ras, MEK, ERK, and MLCK serve as essential downstream effectors.

L15 ANSWER 24 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:339451 BIOSIS
DOCUMENT NUMBER: PREV199900339451
TITLE: Overexpression of protein kinase C-alpha in MCF-7 breast cancer cells results in differential regulation and expression of alphavbeta3 and alphavbeta5.
AUTHOR(S): Carey, Indira; Williams, Carol L.; Ways, D. Kirk; Noti, John D. (1)
CORPORATE SOURCE: (1) Laboratory of Molecular Biology, Guthrie Research Institute, One Guthrie Square, Sayre, PA, 18840 USA
SOURCE: International Journal of Oncology, (July, 1999) Vol. 15, No. 1, pp. 127-136.
ISSN: 1019-6439.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB MCF-7 **breast cancer** cells stably transfected with protein kinase C-alpha (MCF-7-PKC-alpha cells) show anchorage-independent growth and exhibit increased tumorigenicity in nude mice. Since integrins are involved in tumor growth and metastatic spread, we investigated whether integrin expression is differentially regulated in MCF-7-PKC-alpha cells. Fluorescence-activated cell sorting revealed that alphavbeta3 is highly expressed on MCF-7-PKC-alpha cells, but is undetectable on MCF-7V cells (MCF-7 cells transfected with vector only). In contrast, MCF-7-PKC-alpha cells have reduced expression of alphavbeta5. Blocking experiments with antibodies to alphavbeta3 and alphavbeta5 revealed that these receptors are used by MCF-7-PKC-alpha cells to adhere primarily to **vitronectin** and osteopontin. Consistent with heterodimer expression, MCF-7-PKC-alpha cells express increased beta3 and decreased beta5 on their surface. Surface expression of alphav on MCF-7-PKC-alpha cells is unchanged. Western blotting, Northern analysis, and nuclear run-on assays indicated that post-translational mechanisms increase the surface expression of beta3 on MCF-7-PKC-alpha cells. In contrast, reduced beta5 transcription diminishes beta5 surface expression on MCF-7-PKC-alpha cells. These results indicate that overexpression of PKC-alpha in MCF-7 cells alters beta5 and beta3 expression by transcriptional and post-translational mechanisms, respectively, resulting in altered heterodimer expression. These findings suggest that the increased metastatic capacity of tumor cells with elevated protein kinase C levels may result, in part, from modulation of integrin expression.

L15 ANSWER 25 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:306763 BIOSIS

DOCUMENT NUMBER: PREV199900306763
TITLE: Thalidomide up-regulates prostate-specific antigen secretion from LNCaP cells.
AUTHOR(S): Dixon, Shannon C.; Kruger, Erwin A.; Bauer, Ken S.; Figg, William D. (1)
CORPORATE SOURCE: (1) Medicine Branch, National Cancer Institute, 10 Center Drive, Bldg. 10, Room 5A01, Bethesda, MD, 20892 USA
SOURCE: Cancer Chemotherapy and Pharmacology, (May, 1999) Vol. 43, No. SUPPL., pp. S78-S84.
ISSN: 0344-5704.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Thalidomide has been shown to have species- and metabolic-dependent antiangiogenic activity in vitro and in vivo, suggesting its potential in treating human angiogenesis-dependent pathologies such as solid tumors. Based on promising preclinical studies, thalidomide has entered phase II clinical trials for prostate, brain, **breast cancer**, and Kaposi's sarcoma. However, the antiangiogenic mechanism of action is largely unresolved, as are its effects on tumor-associated gene expression, cytokine secretion, etc. We have investigated the effects of thalidomide on: 1) the secretion of prostate-specific antigen (PSA) in a human androgen-dependent prostate cell line; 2) growth and viability of human prostate cells; and 3) differential gene expression profiles of thalidomide-treated vs untreated human prostate cells. A human androgen-dependent prostate carcinoma cell line (LNCaP) and a human androgen-independent prostate carcinoma cell line (PC-3) were incubated with thalidomide 0.6, 6, or 60 mug/mL for 5-6 days. Secreted PSA from LNCaP cells was measured using a commercial enzyme-linked immunosorbant assay. Cell viability studies were conducted in both LNCaP and PC-3 cells using the same thalidomide concentrations. Furthermore, the differential gene expression of thalidomide-treated LNCaP cells was compared to that of untreated control cells using a commercially available human cancer cDNA expression array system. Thalidomide-treated LNCaP cells demonstrated increased PSA/cell levels at all concentrations tested compared to untreated control cells. Thalidomide demonstrated a cytostatic effect in LNCaP cells but had no appreciable effect on PC-3 cell viability compared to untreated control cells. Comparison of cDNA expression arrays hybridized with thalidomide-treated LNCaP cDNA probes suggests that thalidomide may up- or downregulate expression of angiogenesis-related genes, i.e., **vitronectin**, but these differential effects require further verification. Thalidomide over a range of doses has demonstrated nontoxic, cytostatic activity in LNCaP cells and significant upregulation of LNCaP cell PSA secretion in vitro. Furthermore, preliminary data from cDNA nucleic acid arrays of thalidomide-treated LNCaP cells suggest that thalidomide upregulates a potential angiogenic modulatory protein, the **vitronectin** precursor, which may eventually link thalidomide's antiangiogenic activity with modulation of angiogenic vascular integrin pathways.

=> d ibib abs 26-30

L15 ANSWER 26 OF 40 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1998143336 MEDLINE
DOCUMENT NUMBER: 98143336 PubMed ID: 9484807
TITLE: Expression of alphav integrins and **vitronectin** receptor identity in **breast cancer** cells.
AUTHOR: Meyer T; Marshall J F; Hart I R
CORPORATE SOURCE: Richard Dimbleby Department of Cancer Research, St Thomas' Hospital, London, UK.

SOURCE: BRITISH JOURNAL OF CANCER, (1998 Feb) 77 (4) 530-6.
Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980312
Last Updated on STN: 19980312
Entered Medline: 19980305

AB In the present study we have used fluorocytometry and immunoprecipitation to characterize the expression of alphav-containing integrins in a panel of eight human breast cancer cell lines and one normal human mammary epithelial line. We show that the classical **vitronectin** receptor alphavbeta3 is expressed in only one cell line (MDA-MB-231), whereas alphavbeta5 is expressed on all **breast cancer** cell lines and alphavbeta1 is expressed on the majority. Using adherence assays to purified ligands in the presence and absence of function-blocking monoclonal antibodies, we have demonstrated that alphavbeta5 mediates adhesion to vitronectin in the majority of these cells. In one cell line, ZR75-1, alphavbeta1 contributes significantly to adhesion to immobilized vitronectin. The formation of focal adhesions containing the alphav and beta1 subunits on vitronectin is also demonstrated by indirect immunofluorescence.

L15 ANSWER 27 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:406879 BIOSIS
DOCUMENT NUMBER: PREV199800406879
TITLE: Bone sialoprotein supports breast cancer cell adhesion proliferation and migration through differential usage of the alphavbeta3 and alphavbeta5 integrins.
AUTHOR(S): Sung, V.; Stubbs, J. T., III; Fisher, L.; Aaron, A. D.; Thompson, E. W. (1)
CORPORATE SOURCE: (1) VBCRC Breast Cancer Res. Unit, St. Vincent's Inst. Med. Res., 9 Princess Street, Fitzroy 3065 Australia
SOURCE: Journal of Cellular Physiology, (Sept., 1998) Vol. 176, No. 3, pp. 482-494.
ISSN: 0021-9541.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Bone sialoprotein (BSP), a secreted glycoprotein found in bone matrix, has been implicated in the formation of mammary microcalcifications and osteotropic metastasis of human **breast cancer** (HBC). BSP possesses an integrin-binding RGD (Arg-Gly-Asp) domain, which may promote interactions between HBC cells and bone extracellular matrix. Purified BSP, recombinant human BSP fragments and BSP-derived RGD peptides are shown to elicit migratory, adhesive, and proliferative responses in the MDA-MB-231 HBC cell line. Recombinant BSP fragment analysis localized a significant component of these activities to the RGD domain of the protein, and synthetic RGD peptides with BSP flanking sequences (BSPRGD) also conferred these responses. The fibronectin-derived RGD counterpart, GRGDSP (Gly-Arg-Gly-Asp-Ser-Pro), could not support these cellular responses, emphasizing specificity of the BSP configuration. Although most of the proliferative and adhesive responses could be attributed to RGD interactions, these interactions were only partly responsible for the migrational responses. Experiments with integrin-blocking antibodies demonstrated that BSP-RGD-induced migration utilizes the alphavbeta3 **vitronectin** receptor, whereas adhesion and proliferation responses were alphavbeta5-mediated. Using fluorescence activated cell sorting, we selected two separate subpopulations of MDA-MB-231 cells enriched for alphavbeta3 or alphavbeta5 respectively. Although some expression of the alternate alphav integrin was still retained, the alphavbeta5-enriched

MDA-MB-231 cells showed enhanced proliferative and adhesive responses, whereas the alphavbeta3-enriched subpopulation was suppressed for proliferation and adhesion, but showed enhanced migratory responses to BSP-RGD. In addition, similar analysis of two other HBC cell lines showed less marked, but similar RGD-dependent trends in adhesion and proliferation to the BSP fragments. Collectively, these data demonstrate BSP effects on proliferative, migratory, and adhesive functions in HBC cells and that the RGD-mediated component differentially employs alphavbeta3 and alphavbeta5 integrin receptors.

L15 ANSWER 28 OF 40 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1999111061 MEDLINE
DOCUMENT NUMBER: 99111061 PubMed ID: 9815812
TITLE: **Vitronectin** binding to urokinase receptor in human **breast cancer**.
AUTHOR: Carriero M V; Del Vecchio S; Franco P; Potena M I; Chiaradonna F; Botti G; Stoppelli M P; Salvatore M
CORPORATE SOURCE: Istituto Nazionale per lo Studio e la Cura dei Tumori, Via M. Semmola.
SOURCE: CLINICAL CANCER RESEARCH, (1997 Aug) 3 (8) 1299-308. Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990311
Last Updated on STN: 20000303
Entered Medline: 19990225

AB Functional assembly of the plasminogen-dependent proteolytic system on the cell surface requires multiple interactions involving urokinase (uPA), urokinase receptor (uPAR), plasminogen activator inhibitors, and other molecules that mediate cell migration and adhesion. We analyzed the in vitro interaction of uPAR-containing particulate cell fractions with the amino-terminal fragment (ATF) of human urokinase and the matrix-like form of vitronectin. Binding and cross-linking of 125I-labeled ATF to crude membrane extracts from LB6-19 mouse cells overexpressing human uPARs in the presence of 25 nM urea-denatured vitronectin led to the formation of Mr 137,000, 92, 000, and 82,000 covalent complexes. Immunoprecipitation of the preformed cross-linked 125I-labeled complexes with anti-vitronectin, anti-uPA, or anti-uPAR antibodies revealed that the Mr 82,000 and 92, 000 species do contain ATF and vitronectin and identified the Mr 137, 000 species as a ternary complex formed by ATF, uPAR, and vitronectin. A similar electrophoretic pattern was displayed by acid-pretreated membranes extracted from MCF-7 breast carcinoma or HT1080 fibrosarcoma cell lines, as well as a ductal breast carcinoma specimen; the latter exhibited complex formation at concentrations of vitronectin lower than 10 nM. Finally, uPAR-vitronectin interaction was further documented by the decreased reactivity of an anti-uPAR polyclonal antibody to acid-pretreated sections of 10 breast carcinomas that had been preincubated with vitronectin. Our findings highlight the ability of uPAR to interact simultaneously with **vitronectin** and uPA in **breast cancer**, supporting a dynamic coupling of the molecular mechanisms underlying plasminogen-dependent matrix degradation and cell adhesion.

L15 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 10
ACCESSION NUMBER: 1998:48607 HCAPLUS
DOCUMENT NUMBER: 128:126468
TITLE: Attachment characteristics and involvement of integrins in adhesion of breast cancer cell lines to extracellular bone matrix components

AUTHOR(S): van der Pluijm, Gabri; Vloedgraven, Hans; Papapoulos, Socrates; Lowik, Clemens; Grzesik, Wojtek; Kerr, Janet; Robey, Pamela Gehron
CORPORATE SOURCE: Dep. Endocrinology, Univ. Hospital, Leiden, Neth.
SOURCE: Laboratory Investigation (1997), 77(6), 665-675
CODEN: LAINAW; ISSN: 0023-6837
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Evidence is mounting that changes in the ability of cancer cells to adhere to extracellular matrixes play a decisive role in metastatic spread. The mechanism underlying the preference of breast cancer cells to metastasize to bone is, however, poorly understood. The authors investigated the expression and involvement of integrin adhesion receptors in the adhesion of breast cancer cells to bone matrix (constituents) in two in vitro attachment assays using RGD peptides and anti-integrin antibodies. Breast cancer cells adhered rapidly to extracellular bone matrix. Adhesion of most cells to vitronectin, fibronectin, thrombospondin, osteopontin, and the fairly bone-specific bone sialoprotein was inhibited by the 200 .mu.g/mL GRGDS peptide. These data suggest that integrin adhesion receptors can modulate the attachment of breast cancer cells to bone matrix mols. In accordance with these findings, the authors found that .alpha.1-.alpha.5(.beta.1) and .alpha.v(.beta.3) integrins were expressed by mammary carcinoma cells. Highly tumorigenic MDA-MB-231 cells, which form osteolytic metastases in vivo, expressed relatively high levels of .alpha.2.beta.1, .alpha.3.beta.1, .alpha.5.beta.1, .alpha.v.beta.3 integrins, when compared to MCF-7, T47D, and ZR75-1 breast cancer cells. Addn. of function-blocking anti-.alpha.2.beta.1, -.alpha.3.beta.1, -.alpha.5.beta.1, and -.alpha.v.beta.3 antibodies significantly inhibited the adhesion of MDA-MB-231 breast cancer cells to bone matrixes. In conclusion, the data suggest a possible role for .beta.1 and .beta.3 integrin subfamily members in the establishment of skeletal metastases in advanced breast cancer patients. Clearly, functional evidence is required to understand the mechanisms involved in the development of skeletal metastases in breast cancer patients.

L15 ANSWER 30 OF 40 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 97195643 MEDLINE
DOCUMENT NUMBER: 97195643 PubMed ID: 9043016
TITLE: Altered cell-matrix contact: a prerequisite for breast cancer metastasis?.
AUTHOR: Gui G P; Puddefoot J R; Vinson G P; Wells C A; Carpenter R
CORPORATE SOURCE: Department of Surgery, St Bartholomew's Hospital, West Smithfield, London, UK.
SOURCE: BRITISH JOURNAL OF CANCER, (1997) 75 (5) 623-33.
Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970407
Last Updated on STN: 19980206
Entered Medline: 19970321

AB The integrins are receptors that regulate interaction between epithelial cells and the extracellular matrix. Previous studies have shown that a reduction in the expression of the alpha2beta1, alpha3beta1, alpha6beta1, alpha(v)beta1 and alpha(v)beta5 integrins in primary breast cancer is associated with positive nodal status. In order to assess the functional significance of altered integrin expression, primary breast cancer cells were derived from individual patients with known tumour characteristics using immunomagnetic separation. Purified human fibronectin, vitronectin,

laminin and type IV collagen were used to represent the principal extracellular matrix proteins in an in vitro adhesion assay. Primary breast cancer cells from lymph node-positive patients were significantly less adhesive to each of the matrix proteins studied ($P<0.001$, Mann-Whitney U-test). Matrix adhesion of primary breast cancer cells from node-negative patients was inhibited by appropriate integrin monoclonal antibodies ($P<0.001$, paired Wilcoxon test). Adhesion to fibronectin, **vitronectin** and laminin, but not type IV collagen, was influenced by the inhibitor arginine-glycine-aspartate, suggesting that **breast cancer** cell recognition of collagen IV is mediated through alternative epitopes. Weak matrix adhesion correlated with loss of integrin expression in tissue sections from corresponding patients assessed using immunohistochemistry. This study demonstrates a link between altered integrin expression and function in primary breast cancers predisposed to metastasize.

=> d ibib abs 31-34

L15 ANSWER 31 OF 40 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 96161975 MEDLINE
DOCUMENT NUMBER: 96161975 PubMed ID: 8576205
TITLE: The roles of integrins and extracellular matrix proteins in the insulin-like growth factor I-stimulated chemotaxis of human breast cancer cells.
AUTHOR: Doerr M E; Jones J I
CORPORATE SOURCE: Department of Medicine, University of North Carolina, Chapel Hill 27599-7170, USA.
CONTRACT NUMBER: DK 02024 (NIDDK)
DK 07129 (NIDDK)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Feb 2) 271 (5) 2443-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960321
Last Updated on STN: 20000303
Entered Medline: 19960312

AB The effects of insulin-like growth factor I (IGF-I) on the migration of two human breast cancer cell lines, MCF-7 and MDA-231, were examined using a modified Boyden chamber. 10 ng/ml was the optimal IGF-I concentration for stimulation of migration. The majority of IGF-I-stimulated migration in both cell types was due to chemotaxis. MCF-7 cells failed to migrate on membranes coated with gelatin or fibronectin and migrated only in small numbers on laminin. In contrast, when vitronectin- or type IV collagen-coated membranes were used, the MCF-7 cells migrated in large numbers specifically in response to IGF-I but not to 10% fetal calf serum, epidermal growth factor, fibroblast growth factor, or platelet derived growth factor-BB. An IGF-I receptor-blocking antibody inhibited IGF-I-stimulated migration in both cell types. In addition, a blocking antibody to the alpha v beta 5 integrin (a vitronectin receptor) inhibited migration of MCF-7 cells in response to IGF-I through vitronectin but not through type IV collagen. Similarly, blocking antibodies specific for alpha 2 and beta 1 integrins significantly inhibited migration of both cell types through type IV collagen-coated membranes but not through vitronectin-coated membranes. We conclude that: 1) IGF-I stimulates migration of these two cell types through the IGF-I receptor; 2) interaction of **vitronectin** with the alpha v beta 5 integrin or collagen with the alpha 2 beta 1 integrin is necessary for the complete

IGF-I response in MCF-7 cells, and 3) because migration represents an in vitro model for metastatic spread, integrins, extracellular matrix proteins, and IGF-I may play coordinated roles in the metastasis of **breast cancer** in vivo.

L15 ANSWER 32 OF 40 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 13
ACCESSION NUMBER: 1996:597256 HCAPLUS
DOCUMENT NUMBER: 125:244457
TITLE: Identification of a 60-kD antigen associated with malignant growth of human breast tissue
AUTHOR(S): Chatterjee, Amitava; Biswas, Nupur; Choudhuri, S. K.; Mazumder, J.; Chowdhury, Jayasree Roy
CORPORATE SOURCE: Department Biochemistry, Chittaranjan National Cancer Institute, Calcutta, 700 026, India
SOURCE: Oncology (1996), 53(5), 422-425
CODEN: ONCOBS; ISSN: 0030-2414
PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antisera against a novel 60 kDa antigen (P60) were developed using immunomasking strategy which shows malignant growth-related expression in human breast cancer tissue. Cell adhesion assay in the presence of P60 antibody clearly indicates a role for P60 directly or indirectly in adhesion of tumor cells to extracellular matrix protein vitronectin. These results indicate that P60 could be a potential marker to distinguish benign from malignant growth of human breast tissue, and that P60 could be an integrin or a non-integrin receptor, or a receptor-related protein to vitronectin.

L15 ANSWER 33 OF 40 MEDLINE
ACCESSION NUMBER: 96350847 MEDLINE
DOCUMENT NUMBER: 96350847 PubMed ID: 8727100
TITLE: Integrin alpha V beta 3 expression by bone-residing breast cancer metastases.
AUTHOR: Liapis H; Flath A; Kitazawa S
CORPORATE SOURCE: Department of Pathology, Washington University School of Medicine, St. Louis, Missouri, USA.
SOURCE: DIAGNOSTIC MOLECULAR PATHOLOGY, (1996 Jun) 5 (2) 127-35.
Journal code: 9204924. ISSN: 1052-9551.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961025
Last Updated on STN: 19961025
Entered Medline: 19961016
AB Breast cancer metastasis to bone is a multistep process requiring attachment of tumor cells to the bone and bone marrow environment. The precise adhesion molecules involved in skeletal homing of breast cancer to bone are unknown but likely include integrins. We investigated the expression of **vitronectin** receptor (alpha V beta 3) by **breast cancer** cells residing in bone because this heterodimer mediates osteoclast-bone recognition. We used immunohistochemistry and in situ hybridization in a systematic study of 22 bone biopsies containing breast cancer metastases and available samples of corresponding primary tumors and normal breast and compared alpha V beta 3, alpha 2 beta 1, and alpha B beta 5 integrin expression. The results showed that alpha V beta 3 was strongly expressed by normal breast epithelium and was decreased in some and strongly expressed in other primary invasive breast carcinomas. In contrast, this integrin heterodimer was abundant in all breast cancer cells metastatic to bone.

In situ hybridization revealed high levels of steady-state mRNA corresponding to sites of protein expression; alpha 2 beta 1 was weakly expressed in both primary and metastatic tumors, and alpha V beta 5 was not detected. Our results showed an overexpression of alpha V beta 3 by bone-residing breast cancer cells and suggest either subclonal selection of alpha V beta 3-expressing tumor cell populations or upregulation of alpha V beta 3 in the bone microenvironment.

L15 ANSWER 34 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:87401 BIOSIS
DOCUMENT NUMBER: PREV199698659536
TITLE: Coexpression of **vitronectin** receptor (alpha-v-beta-3), 92-kD (MMP-9), and 72-kD (MMP-2) metalloproteinases in **breast cancer** metastasis to bone.
AUTHOR(S): Liapis, H.; Flath, A.; Sudbeck, B. D.
CORPORATE SOURCE: Washington Univ. Med. Cent., Dep. Pathol., St. Louis, MO USA
SOURCE: Pathology Research and Practice, (1995) Vol. 191, No. 7-8, pp. 713-714.
Meeting Info.: XVth European Congress of Pathology Copenhagen, Denmark September 3-8, 1995
ISSN: 0344-0338.
DOCUMENT TYPE: Conference
LANGUAGE: English

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